by manual endocardial tracing of 8 equidistant parallel LV short axis slices for 3DE, while for MRI 9-mm slice thickness was used. Data were analyzed by two independent observers and the first observer analyzed the data twice with one week interval. A second 3DE acquisition was performed after one week for DD variability.

Results: The mean ± SD of ED- and ES-LVV (ml) and EF (%) for MRI were (113 ± 16, 47 ± 6 and 58 ± 5) and (225 ± 70, 168 ± 64 and 27 ± 12), while for 3DE were (110 ± 16, 47 ± 6 and 60.5) and (226 ± 65, 171 ± 63 and 25 ± 11) for A and B groups, respectively. Variabilities of both techniques expressed by SEE% (table).

		3DE			MRI		
		EDV	ESV	EF	EDV	ESV	EF
Intra. SEE	A	3.0	5.1	3.4	6.5	6.4	3.3
	B	3.3	3.1	0.6	3.9	3.2	1.2
Inter. SEE	A	6.6	6.8	5.8	10.6	7.5	9.8
	B	3.9	2.5	0.9	15.2	14.7	2.0
DD SEE	A	3.4	1.4	2.3			
	B	1.5	1.0	2.7			

Conclusions: 3DE has a small intra- and interobserver as well as day to day variabilities for LVV and EF calculation in both normal subjects and patients with impaired LV function. Observer variabilities of 3DE are at least similar to that of MRI for LVV and EF calculation in both A and B groups.

11:00

705-3 Left Ventricular Ejection Fraction in Patients With Normal and Distorted left ventricular Geometry: Three-Dimensional Echocardiography Versus Biplane Modified Simpson's Method With Comparison to Radionuclide Angiography

Y.F.M. Nosir, W.B. Vletter, R.T. vanDomburg, A. Salustri, R. Frowijn, J. Tjoa, A.E.M. Reijs, P.M. Fioretti, F.J. Ten Cate, J.R.T.C. Roelandt. *AZR, Thoraxcenter, Rotterdam, The Netherlands*

Our aim was to compare left ventricular ejection fraction (LVEF) calculated by three-dimensional echocardiography (3DE) and biplane modified Simpson's method (BMS) with values obtained from radionuclide angiography (RNA).

Methods: 29 unselected patients referred for RNA underwent precordial 3DE using rotational acquisition of 90 cut-planes with ECG and respiratory gating. From the volumetric dataset LVEF was calculated by, (a) 3DE using Simpson's rule at 3-mm slice thickness and (b) biplane modified Simpson's method (BMS) using two orthogonal apical long axis views. Patients were divided into three groups, (A) 12 patients with segmental wall motion abnormalities (WMA), (B) 6 patients with LV global hypokinesis (GH) and (C) 11 patients with normal LV wall motion (N). Observer variability was calculated for all techniques.

Results: Mean ± SD of LVEF calculated by RNA, 3DE and BMS were 39 ± 20, 38 ± 19 and 38 ± 19, respectively. There were excellent correlation between LVEF calculated by both 3DE and BMS and values obtained by RNA (r = 0.99 and 0.97), respectively. The limits of agreement tended to be closer between 3DE and RNA (−6.8, +7.2) (P = 0.7) than between BMS and RNA (−8.3, +9.7) (P = 0.5). The intraobserver and interobserver variability of RNA, 3DE and BMS for calculating LVEF were (0.8 and 1.5), (1.3 and 1.8) and (1.6 and 2.6), respectively. There were better correlation for LVEF calculation between 3DE and RNA in A, B and C subgroup (r. = 0.99, 0.99 and 0.83), than between BMS and RNA (r. = 0.93, 0.97 and 0.77), respectively. There were closer limits of agreements between 3DE and RNA for LVEF calculation in A, B and C patients subgroup {(−3.5, +5), (−8.4, +5.6) and (−7.8, +8.6)}, than that between BMS and RNA {(−8.1, +10.7), (−11.9, +9.3) and (−9.1, +11.3)}, respectively.

Conclusions: 3DE has better correlation and closer limits of agreement than BMS with RNA for LVEF calculation particularly evident in patients with segmental WMA and GH (group A and B). 3DE has similar observer variability of RNA. Therefore we recommend to use 3DE for serial accurate LVEF calculation of cardiac patients.

11:15

705-4 Rapid Image Acquisition and Automated Determination of Left Ventricular Cavity Boundary for Precise and Accurate Volumetry by Clinical Three-Dimensional Echocardiography

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Data acquisition for three-dimensional (3D) echocardiography is usually time consuming. Clinical ultrasound images of the left ventricle (LV) are usually hampered by noise and signal attenuation causing dropouts in the LV endocardial boundary. We have developed a quick image acquisition technique that allows collection of serial tomograms within approximately 6 seconds. The resulting data set is suitable for gross-anatomical 3D reconstruction of the LV. A trainable computer algorithm, involving neural network techniques that gain knowledge about LV shape from expert outlines, has been developed to automatically map endocardial surface using spatially located nodes (vertices). The objective of this research was to test precision and accuracy of the method in artifact-prone clinical 3D echocardiograms. Expert endocardial outlines in serial echocardiographic images from 11 patients with various LV geometries were used for training of the computer 3D neural network algorithm. Another group of 10 patients with echocardiograms containing noise and image dropouts was used to test the performance of the system. The knowledge-based computer system appropriately identified endocardial surface in various, artifact-prone echocardiographic images. Estimated LV diastolic and systolic volumes were compared to those calculated from expert outlines. The comparison showed correlation coefficient >0.96 at $p < 0.001$, standard deviation < ±5.75 ml, root mean squared error <6.08 ml, negative bias <2.4 ml, and variability <6.46%. In conclusion, rapid image acquisition is clinically feasible and the knowledge-based, 3D endocardial surface recognition technique ("a trainable computer expert"), which capitalizes on 3D relationship of nodes, provide precise and accurate assessment of LV volumes in patients with various LV geometries.

11:30

705-5 Three-Dimensional Echocardiography by Rapid Free Scanning From Multiple Transthoracic Windows

D. Leotta, B. Munt, M. Legget, R. Martin, X.-N. Li, E. Bolson, T. Zwink, C. Kraft, G. Bashein, M. Sivarajan, C. Otto, F. Sheehan. *University of Washington, Seattle, WA, USA*

Three-dimensional (3D) echocardiography has recently been shown to improve the accuracy and reproducibility of estimates of left ventricular (LV) mass and volume. However, accuracy of 3D cardiac reconstructions can be limited by such factors as lengthy image acquisition times, limited acoustic viewing windows, a need for respiratory gating, and geometric assumptions of LV shape.

We present a method for quickly acquiring a 3D scan using a commercial ultrasound scanner equipped with a magnetic position locating device (Ascension Technology Flock of Birds). Digital images are captured continuously while freely tilting, translating and/or rotating the probe. In four breath holds of eight seconds each, complete scans from the parasternal (short and long axis) and apical windows are obtained.

The digital image files are linked to their spatial coordinates and the electrocardiogram. Object borders are manually traced using custom software that allows interactive 3D visualization and editing of the outlines. The scanned objects are reconstructed using a piecewise-smooth subdivision surface-fitting algorithm.

Phantom imaging indicates that the system accurately reproduces volume (true volume = 0.96 calculated volume + 2.2 ml, $r^2 = 0.999$, SEE = 1.0 ml, n = 14 balloons) and shape (rms distance of reconstructed surface to ideal surface <1 mm, n = 3 cylinders). Initial scans in ten normal subjects indicate that LV reconstructions are feasible in awake patients. These results suggest that LV volume and shape can be calculated accurately from images acquired during rapid free scanning *in vivo*. With this technique, images are acquired quickly from one or more acoustic windows without respiratory gating, and reconstructions of the LV are performed without geometric assumptions.

11:45

705-6 Manual and Semiautomated Measurement of Left Ventricular Volume Using Real-Time, Three Dimensional Echocardiography in Vivo

T. Ota, C.E. Fleishman, C. Ohazama, G. Stetten, C. Lewis, D.D. Glower, T. Ryan, O.T. von Ramm, J. Kisslo. *Duke University Medical Center, Durham, NC, USA*

To test the hypotheses that left ventricular volume (VOL) could be calculated by real-time, three-dimensional echocardiography (RT3D) and a semiautomated border detection method (SEMI) was possible, images from 9 closed chested dogs were analyzed for end-systolic volume (ESV), end-diastolic volume (EDV), stroke volume (SV), and ejection fraction (EF) using the Duke University RT3D device. The system uses a matrix phased array transducer (2.5 MHz) to scan a 65º pyramidal volume at 22 vol/s and allows for capture of an entire cardiac cycle for later analysis. Myocardial contrast enhancement was obtained by LA injection of 2% activated dodecafluoropentane. EDV and ESV were determined by Manual (MAN) tracing of endocardial borders from sequential inclined C-scans (parallel to the transducer face) 4 mm apart from the looped data using Simpson's rule. SEMI VOL was calculated on the same images. Nearly simultaneous LV single plane angiograms (ANGIO)

were obtained and ANGIO VOL calculated by area-length method. The SEMI VOL correlated well with the MAN VOL, for EDV: $y = 0.94 \times +4.66$ ($r^2 = 0.94$), for ESV: $y = 1.13 \times -1.91$ ($r^2 = 0.92$).

Compared VOL data from RT3D and ANGIO are shown below (mean ± SD).

	EDV (ml)	ESV (ml)	SV (ml)	EF (%)
RT3D (MAN)	42.2 ± 13.4	22.2 ± 10.8	20.6 ± 6.2	48.8 ± 11.3
RT3D (SEMI)	46.9 ± 13.7	26.0 ± 13.6	21.1 ± 6.6	46.2 ± 13.9
ANGIO	41.2 ± 11.2	20.6 ± 8.6	20.1 ± 3.7	50.1 ± 7.3

The regression at EDV of MAN vs. ANGIO was $y = 1.16 \times -4.13$ ($r^2 = 0.95$), SEMI vs. ANGIO was $y = 1.01 \times +4.14$ ($r^2 = 0.92$). At ESV, corresponding regressions were MAN $y = 1.13 \times -0.76$ ($r^2 = 0.82$) and SEMI $y = 1.14 \times +1.19$ ($r^2 = 0.71$). These data indicated that LV VOL calculated by RT3D using MAN correlated well with ANGIO VOL. The SEMI method is currently less precise in vivo. These findings are an important step to automated beat-to-beat RT3D VOL analysis.

706 Vascular Pharmacology

Monday, March 17, 1997, 10:30 a.m.–Noon
Anaheim Convention Center, Room B2

MONDAY ORAL

10:30

706-1 Effects of Acute Angiotensin-Converting Enzyme Inhibition on Peripheral Vasodilator Responses to Bradykinin and Acetylcholine in Healthy Subjects and Patients with Coronary Artery Disease

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The aim of the study was to assess the effects of local and acute inhibition of angiotensin-converting enzyme (ACE) on vasodilation to acetylcholine (ACh) and bradykinin (BK) in 9 healthy subjects compared to 10 patients (pts) with coronary artery disease (CAD). Forearm blood flow (FBF) was measured by venous occlusion plethysmography during infusion of ACh (40, 80 μg/min) and BK (10, 30, 100 pmol/min) into the brachial artery with or without quinalaprilat (Q) (50 μg/min). Vasodilation (percent change) was decreased in pts compared to controls with BK (260 ± 42% vs 482 ± 52%, $p < 0.05$) but not with ACh (243 ± 74% vs 341 ± 67%, NS). Q alone did not affect FBF in any group. Coinfusion of Q with BK enhanced BK-induced vasodilation in controls (620 ± 48% vs 482 ± 52%, $p < 0.05$) and in patients (506 ± 67% vs 260 ± 42%, $p < 0.05$). For ACh, Q enhanced ACh-induced vasodilation in controls (494 ± 100% vs 341 ± 67%, $p < 0.05$) but not in pts (233 ± 54% vs 243 ± 74%, NS). LNMMA (8 μmol/min), a specific inhibitor of NO-synthase, did not inhibit BK-induced vasodilation. *Conclusion:* In patients with CAD, although peripheral vasodilation to BK is blunted, ACE inhibitors are able to enhance BK-induced vasodilation in the same extent than in controls. This vasodilation is probably distinct from NO pathway.

10:45

706-2 Reduced Nitric Oxide-Dependent Forearm Vasodilation in Normotensive Blacks Compared to Whites

C. Cardillo, C.M. Kilcoyne, A.A. Quyyumi, R.O. Cannon, III, J.A. Panza. *NHLBI, Bethesda, MD, USA*

The physiologic basis of the increased susceptibility of blacks to hypertension and its complications is unknown. Given the important role of endothelium-derived nitric oxide (NO) in the regulation of vascular tone and in the protection against atherosclerosis, we hypothesized that NO activity could be impaired in blacks. To test this hypothesis, we studied the forearm blood flow (FBF) response (strain-gauge plethysmography) to intraarterial infusion of acetylcholine (ACh; 7.5, 15 and 30 μg/min), an endothelium-dependent vasodilator, and sodium nitroprusside (SNP; 0.8, 1.6 and 3.2 μg/min), an exogenous NO donor given to test the intrinsic endothelium-independent vasodilator capacity of the vessel wall, in 12 normotensive whites (5 men) and 11 normotensive blacks (5 men) approximately matched for age. No significant difference was observed between whites and blacks in baseline FBF (3.1 ± 0.6 vs 2.9 ± 1.2 mL/min/dL, respectively; $P = 0.59$). The response to ACh was significantly reduced in blacks compared to whites (maximum flow: 6.7 ± 3 vs 14.4 ± 3.7 mL/min/dL, respectively; $P < 0.001$). Of note, the response to SNP was also significantly blunted in blacks (maximum flow: 6.9 ± 2 vs 11.3 ± 3.4 mL/min/dL in whites; $P < 0.001$), indicating that the observed difference in the response to ACh is likely to be due not to impaired NO generation but to impaired responsiveness of vascular smooth muscle cells to the vasorelaxing effect of NO. This abnormality may contribute to the increased prevalence of hypertension and the higher incidence of cardiovascular complications in blacks.

11:00

706-3 Safety and Efficacy of Nitric Oxide and Adenosine in Predicting Nifedipine Response in Primary Pulmonary Hypertension

M.J. Ricciardi, B.P. Knight, M. Rubenfire. *University of Michigan, Ann Arbor, MI, USA*

Primary pulmonary hypertension (PPH) has limited treatment options including calcium blockers, IV prostacyclin, and lung transplant. A trial with incremental dosing of oral nifedipine (nif), 20 mg/hr for 8 hrs or intolerance, can identify PPH patients who are nif responders, defined as ≥20% fall in mean pulmonary artery pressure (mPA) or pulmonary artery resistance (PAR). Nif trials carry a risk of profound hypotension and death. Response to IV adenosine (aden), 50 μg/kg q 2 min up to 500 μg/kg/min or intolerance, is reportedly a safe predictor of nif response. Inhaled nitric oxide (NO), 80 ppm for 5 min, may have similar value. We studied the safety and accuracy of predicting nif response with NO in 15 and aden in 13 of 19 PPH pts scheduled to undergo a nif trial the following day. Vasoactive drugs were withheld for 24 hrs. Average age was 43 ± 14 yrs, 74% women. Baseline mRA 13 ± 9 mmHg, mPA 56 ± 11 mmHg, CO 4.6 ± 2 L/min, and PAR 10.2 ± 5.0 Wood units. Nine pts received both NO and aden. The mean peak aden rate was 204 μg/kg/min (range 100–400). Ten of the 19 pts responded to nif. All 15 pts tolerated NO although 2 had transient arterial desaturation. Seven of 15 (46.6%) responded to NO of which 6 responded to nif. The 8 NO non-responders did not respond to nif. NO correctly predicted nif response in 14 of 15 pts (93.3%). All NO responders tolerated nif without complications. Six of 13 pts (46.1%) were aden responders of which 3 responded to nif. Of 7 non-responders to aden, 2 responded to nif. Aden predicted nif response in 8 of 13 pts (61.5%). Three aden responders suffered adverse effects with nif (hypotension in 2, shock and death in 1). Agreement between NO and aden was poor (Kappa 0.18).

In summary, NO predicts nif response (93% predictive accuracy) and nif trial safety. In contrast aden, in the dosing schedule used, is less predictive of nif response (61%), p.045 by McNemar's, and may encourage high risk and unnecessary nif trials.

11:15

706-4 Ergotamine Limits Hyperemic Myocardial Blood Flow in Humans

T. Gnecchi-Ruscone, R. Lorenzoni, F. Hermansen, N. Legg, D. Tousoulis, G. Shepherd [1], P.G. Camici. *MRC Clinical Sciences Centre, Royal Postgraduate Medical School, Hammersmith Hospital, London, UK,* [1] *GLAXO-Wellcome Ltd, Greenford, UK*

Although ergotamine (E) is beneficial for migraine it may cause myocardial ischemia. Aim of this study was to ascertain whether E affects myocardial blood flow (MBF) in humans. A double blind randomized, placebo (P) controlled, crossover study was performed in 15 migraineurs (age 54 ± 4, 4 males) with no history of ischemic heart disease, normal echocardiogram and negative stress test at high workload. MBF (ml/g/m) was measured with positron emission tomography and ^{15}O labelled water at baseline (bas) and after intravenous dipyridamole (dip; 0.56 mg/kg). Bas and dip MBF were measured twice, i.e. after intravenous E (0.25 mg) or P, on two different days. Bas hemodynamic and MBF data after P and E were not significantly different. By contrast, E led to significant changes in dip-MBF, coronary vasodilator reserve (CVR, dip-MBF/bas-MBF) and minimal coronary resistance (min-CR, mean dip-pressure/dip-MBF, mmHg/ml/m/g).

	bas-MBF	dip-MBF	CVR	min-CR
P	1.45 ± 0.31	3.72 ± 1.05	2.71 ± 1.15	27 ± 8
E	1.44 ± 0.41	2.62 ± 1.1*	1.81 ± 0.5*	42 ± 1*

Data are shown as mean ± SD. (*$p < 0.01$, P vs E).

Conclusions: E significantly reduces near maximal coronary vasodilation in human subjects without history of ischemic heart disease, probably through activation of coronary serotonergic and/or α_1-adrenergic receptors. This could explain the ischemic effect of E in the heart.